Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 17, 27, and 56 have been amended to recite that the "contacting" step "reduces CD40 ligand release." Descriptive support for this limitation is provided at page 15, lines 4-27, and Example 6 (citing Figures 6A-B). Therefore, no new matter has been introduced by these amendments. Claims 17-37, 56-65, and 106-108 remain pending and under examination. No excess claim fees are due with this submission.

This submission is accompanied by a request for a five-month extension of time (from the deadline of November 14, 2009, for filing of an appeal brief) and a request for continued examination (RCE). Fees for the extension of time and RCE have been withdrawn from deposit account 14-1138. Any excess fees can be credited and any fee deficiencies can be charge to this same account.

The rejection of claims 27-37 under 35 U.S.C. § 112, first paragraph, for lack of enablement is overcome by the amendments to claim 27.

The rejection of claims 23-25, 33-35, and 62-65 under 35 U.S.C. § 112, second paragraph, for indefiniteness is respectfully traversed.

Claim 17 recites the step of "contacting mammalian platelets with an effective amount of … a PPARγ agonist…," claim 27 recites "contacting mammalian platelets…by administering to the individual an effective amount of … a PPARγ agonist…," and claim 56 recites "contacting mammalian platelets with an effective amount of … a PPARγ agonist…." Claims 23, 33, and 62 depend from claims 17, 27, and 56, respectively, and recite an *additional* step that provides for said contacting, *i.e.*, allows the contacting step to occur. This additional step comprises "administering … an inducer of a PPARγ agonist to a mammal …" or "administering … an inducer of a PPARγ agonist to the individual …." As explained in the specification at page 16, lines 26-30, an inducer of a PPARγ agonist is an agent that induces an increase in the expression or production of a native PPARγ agonist. Because the administering of an inducer of a PPARγ agonist to a mammal/individual in accordance with claims 23, 33, and 62 is one way to carry out the contacting step of claims 17, 27, and 56 (when using a PPARγ agonist), the "inducer of a PPARγ agonist" need not be

listed in these independent claims. Rather, proper antecedent basis for *an* inducer of a PPARγ agonist is recited in claims 23, 33, and 62; and dependent claims 24, 34, and 63 properly refer to "*the* inducer of a PPARγ agonist". Because the position asserted by the PTO is incorrect, in view of the claim language presented, this rejection should be withdrawn.

The rejection of claims 17-23, 25, 27-33, 35, 37, 56-62, and 64 under 35 U.S.C. § 103(a) for obviousness over the combination of U.S. Patent No. 6,127,394 to Pershadsingh et al. ("Pershadsingh") in view of U.S. Patent No. 7,018,985 to Boyer et al. ("Boyer") is respectfully traversed.

Pershadsingh identifies a class of thiazolidinedione derivatives and indicates that the compounds are activators of PPARγ (col. 11, line 13), although other portions of the reference are unclear whether these compounds are agonists or antagonists of PPARγ (col. 11, lines 13-14, reciting that assay "can be used to screen for PPARγ *antagonist*" (emphasis added)). Among a remarkably long list of disparate indications (over 200 diseases or conditions listed in Tables II-VII), Pershadsingh identifies "thrombosis and restenosis after angioplasty" and "myocardial infraction" in Table II. There is, however, no experimental evidence cited in Pershadsingh to support either of these uses, nor is there any reference to prior art support for these therapeutic uses with related compounds (i.e., other thiazolidinediones). In other words, Pershadsingh provides no scientific basis or reasoning to support an expectation that the class of thiazolidinedione derivatives would, in fact, be useful for these two indications (let alone many of the other indications).

Boyer is cited primarily as background evidence, which the PTO relies on to demonstrate that platelet adhesion and activation were known to be critical events in intravascular thrombosis.

Based on the combination of Pershadsingh and Boyer, the PTO asserts at pages 8-9 of the office action that the treatment of thrombosis as described by Pershadsingh would have involved prevention of platelet activation and aggregation, as taught by Boyer. Applicants respectfully disagree.

Prior to the present invention, it was not known that platelets possessed the nuclear receptor PPARγ. Quite the contrary, persons of skill in the art would have expected that platelets did not possess PPARγ, because platelets lack a nucleus. Given this expectation, persons of skill in the art would have had no basis whatsoever to expect that contacting a platelet with a PPARγ agonist would have any effect at all. Indeed, the present

invention involved the identification of a surprising, new non-transcriptional function for PPARγ. The present application demonstrates for the first time that contacting a platelet with a PPARγ agonist can inhibit platelet release of CD40 ligand (as well as thromboxanes and prostaglandins), and also inhibit expression of CD40 ligand on the platelet surface. None of these changes in platelet activity would have been expected by persons of skill in the art given the prior expectation that platelets do not possess the nuclear receptor PPARγ.

The PTO acknowledges at page 9 that Pershadsingh fails even to mention platelets. In fact, the word 'platelet' only appears in the specification of Pershadsingh in the context of conducting blood work to assess a hypothetical patient profile, e.g., "[a]dditionally, a complete blood count, including white cell count and differential, platelet count, and liver function tests…are checked prior to treatment and periodically thereafter" (Example 4, col. 21, lines 4-8). This is mentioned only in the *prospective* examples of Pershadsingh. Thus, Pershadsingh does not contemplate contacting platelets with the PPARγ agonist as claimed.

Moreover, to the extent that the PTO considers the administering of PPARγ agonists as described in Pershadsingh to be the same process as that claimed (see Office Action at page 9), applicants submit that the presently claimed invention is nevertheless patentable because it is directed to a different purpose from Pershadsingh.

It is a well established basis of patent law that new uses of known products or processes are patentable. *See* 35 U.S.C. § 101 (2010) ("Whoever invents or discovers any new and useful process … may obtain a patent therefore…."); 35 U.S.C. § 100(b) (2010) ("The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."). Whether or not a new use of a known process is patentable depends on whether or not the known process is "directed *to the same purpose*" as previously known uses. *See Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1376, 58 USPQ2d 1508, 1514 (Fed. Cir. 2001) (emphasis added). In *Bristol-Myers*, the Federal Circuit held that claims directed to methods of treating patients for taxol-sensitive tumors by administering a certain dosage of taxol to a patient over about three hours, either with or without pretreatment of the patient for reduction of hypersensitivity to taxol, were inherently taught by a reference that reported phase I testing of taxol, using dosages and time constraints as claimed, and suggested pretreatment of patients to reduce their hypersensitivity. Importantly, the court noted that the claimed methods were *for the same purpose* as the known process described in the prior art (*id.*), and

the claimed methods did not require a particular result of the recited steps (246 F.3d at 1372-73, 1378; 58 USPQ2d at 1514, 1515).

In contrast to the holding in *Bristol-Myers*, the presently claimed subject matter is being carried out for a different purpose, namely reducing CD40 ligand release and inhibiting aggregation of the mammalian platelets. This is also different from the hundreds of indications listed in Pershadsingh, including "thrombosis and restenosis after angioplasty" and "myocardial infraction." There is no identification in Pershadsingh whether the allegedly treatable indications are mediated via known anti-inflammatory effects of the disclosed PPARγ agonists or some other mechanism.

The mere possibility that the treatment of "thrombosis and restenosis after angioplasty" or "myocardial infraction" may be mediated via the known anti-inflammatory effects of the disclosed class of thiazolidinedione compounds of Pershadsingh means that the claimed invention cannot be considered to be taught inherently by the combination of Pershadsingh and Boyer. Indeed, "[i]nherency … may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (CCPA 1981) (quoting *Hansgirg v. Kemmer*, 102 F.2d 212, 214, 40 U.S.P.Q. 665, 667 (CCPA 1939) (emphasis added)); *see also Trintec Indus. Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 12957, 63 U.S.P.Q.2d 1597, 1601 (Fed. Cir. 2002) ("Inherency does not embrace probabilities or possibilities."). To support a rejection under principles of inherency, the PTO must provide evidence or scientific reasoning to show that the missing limitations are necessarily present. *See Ex parte Whalen*, 89 U.S.P.Q.2d 1078, 1083 (Bd. Pat. App. & Interf. 2008). Such evidence or scientific reasoning is lacking in the office action (and Pershadsingh).

Given the expectation that PPARγ was not expressed in platelets and the absence of any teaching whatsoever in Pershadsingh concerning the ability of PPARγ agonist to blunt the activity of platelets, persons of skill in the art would not have expected the contacting of platelets with a PPARγ agonist to be useful for reducing CD40 ligand release and either inhibiting platelet aggregation, inhibiting platelet activation (to treat a thrombotic condition or disorder), or inhibiting thrombus formation as presently claimed. That platelet activation is involved in thrombus formation—the reason for the PTO's reliance on Boyer—is beside the point. There simply was no expectation in the prior art that the claimed invention could be achieved in the manner claimed, *i.e.*, by contacting platelets with a PPARγ agonist.

Moreover, as further evidence of the nonobviousness of the presently claimed invention, applicants again direct the attention of the PTO to two post-filing date references that recognize the substantial contribution of the present invention. Santilli et al., "CD40/CD40L System and Vascular Disease," *Intern Emerg Med.* 2:256-268 (2007) ("Santilli," copy attached as Exhibit 1 to November 26, 2008 response) and Borchert et al., "Review of Pleiotropic Effects of Peroxisome Proliferator-Activated Receptor γ Agonists on Platelet Function," *Diabetes Technology & Therapeutics* 9(5):410-420 (2007) ("Borchert," copy attached as Exhibit 2 to November 26, 2008 response). Santilli recites, at page 262, that the work of the present inventors "identify[ies] in the platelet a *new* target cell for [thiazolidinediones]" (emphasis introduced). Borchert credits the present inventors as the first to discover that platelets contain large amounts of PPARγ protein.

Because the discovery underlying the present invention represents a paradigm shift in the understanding of platelet function, persons of skill in the art would have recognized at the time the present invention was made—and, indeed, have since—that the platelet represents a new target for PPARγ agonists. As such, persons of ordinary skill in the art would not have expected before October 2003 that contacting mammalian platelets with a PPARγ agonist would "inhibit[] formation of a thrombosis by the mammalian platelets" (claim 17), "inhibit[] platelet activation to treat the thrombotic condition or disorder" (claim 27), or "inhibit[] aggregation of the mammalian platelets" (claim 56).

For these reasons, the obviousness rejection of claims 17-23, 25, 56-62, and 64 over the combination of Pershadsingh in view of Boyer is improper and should be withdrawn.

The rejection of claims 24, 26, 34, 36, 63, and 65 under 35 U.S.C. § 103(a) for obviousness over the combination of Pershadsingh and Boyer, as cited above, further in view of U.S. Patent No. 6,413,931 to Höök et al. ("Höök") is respectfully traversed.

The teachings and deficiencies of the combination of Pershadsingh and Boyer are noted above. Höök describes the use of decorin to bind fibrinogen in the presence of zinc (Zn^{2+}) to prevent fibrin clot formation. The PTO has asserted that one of skill in the art would have used decorin to treat thrombosis given the teachings of Höök. Applicants respectfully disagree for several reasons.

Firstly, Höök fails to overcome the above-noted deficiency of the combination of Pershadsingh and Boyer.

Secondly, the claim language requires "administering … an inducer of a PPARγ agonist to a mammal in a manner that *provides for said contacting*" (claims 23 and 62) or administering a DNA molecule encoding the inducer, which also is "*effective to cause said contacting*" (as recited in claims 26, 36, and 65). Thus, the use of an inducer of a PPARγ agonist, such as decorin, or a DNA molecule encoding the same, is not for directly acting on fibrinogen as described by Höök, but instead for the entirely different purpose of inducing production of a native PPARγ agonist, which in turn contacts the platelets. Because Höök fails to teach or suggest this new use of decorin or a DNA molecule encoding decorin, the combination of Pershadsingh, Boyer, and Höök is deficient in this regard.

For these reasons, the rejection of claims 24, 26, 34, 36, 63, and 65 for obviousness over the combination of Pershadsingh, Boyer, and Höök is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

Date: April 14, 2010

/Edwin V. Merkel/
Edwin V. Merkel
Registration No. 40,087

Nixon Peabody LLP
1100 Clinton Square
Rochester, New York 14604
Telephone: (585) 263-1128
Facsimile: (585) 263-1600